

(19) World Intellectual Property
Organization
International Bureau



28 JAN 2005



(43) International Publication Date
5 February 2004 (05.02.2004)

PCT

(10) International Publication Number
WO 2004/011012 A3

(51) International Patent Classification⁷: **A61K 35/14**,
35/28, 35/50, 35/44

(21) International Application Number:
PCT/CA2003/001098

(22) International Filing Date: 29 July 2003 (29.07.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/398,791 29 July 2002 (29.07.2002) US
60/435,294 23 December 2002 (23.12.2002) US

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicants (*for all designated States except US*): **ASAHI KASEI KABUSHIKI KAISHA** [JP/JP]; 2-6, Dojima-hama 1-chome, Kita-ku, Osaka-shi, Osaka 530-8205 (JP). **ROBARTS RESEARCH INSTITUTE** [CA/CA]; 100 Perth Drive, London, Ontario N6A 5K8 (CA).

(72) Inventor; and

(75) Inventor/Applicant (*for US only*): **BHATIA, Mickie** [CA/CA]; 23 Penrith Crescent, London, Ontario N6G 4M8 (CA).

(74) Agent: **BERESKIN & PARR**; 40 King Street West, 40th Floor, Toronto, Ontario M5H 3Y2 (CA).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
25 March 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **STEM CELLS FOR TREATING PANCREATIC DAMAGE**

(57) Abstract: Methods and compositions for treating hyperglycemia and pancreatic damage as well as stimulating the repair or regeneration of islet cells are disclosed.

WO 2004/011012 A3

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/A 03/01098

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K35/14 A61K35/28 A61K35/50 A61K35/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 11011 A (REYES MORAYMA ; FURCHT LEO T (US); VERFAILLIE CATHERINE M (US)) 15 February 2001 (2001-02-15) cited in the application page 1, line 26 page 8, line 23 - page 9, line 22 page 14, line 22 - line 25 page 45, line 16 - line 26 page 51, line 6 - page 52, line 17 ---	1-28
P, X	WO 02 064748 A (FURCHT LEO T ; VERFAILLIE CATHERINE M (US)) 22 August 2002 (2002-08-22) page 9, line 29 - page 13, line 5 page 21, line 23 - page 22, line 2 page 32, line 6 - line 9 page 39, line 25 - line 28 claims 3, 20, 27, 29, 35, 52, 54, 57, 59, 61, 68, 73 --- -/--	1-28

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

12 January 2004

Date of mailing of the international search report

23/01/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Schnack, A

INTERNATIONAL SEARCH REPORT

International Application No

PC 03/01098

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, Y	EP 1 254 952 A (KYOWA HAKKO KOGYO KK) 6 November 2002 (2002-11-06) '0017!-'0025! ----	1-28
X	US 5 780 299 A (AMBESI-IMPIOMBATO FRANCESCO SA ET AL) 14 July 1998 (1998-07-14) *entire document, especially the claims* ----	1-28
P, X	WO 02 083187 A (ISLET TECHNOLOGY INC) 24 October 2002 (2002-10-24) page 21, line 6 -page 23, line 21 page 35, line 21 -page 37, line 9 *examples and claims* ----	1-28
P, X	HESS, DAVID ET AL: "Bone marrow-derived stem cells initiate pancreatic regeneration" NATURE BIOTECHNOLOGY (2003), 21(7), 763-770 , 2003, XP002265780 *entire document* ----	1-28
A	ORTIZ, MARIAESTELA ET AL: "Functional characterization of a novel hematopoietic stem cell and its place in the c-kit maturation pathway in bone marrow cell development" IMMUNITY (1999), 10(2), 173-182 , 1999, XP001156831 *entire document* ----	1-28
Y	SPRINGER, MATTHEW L. ET AL: "Not the usual suspects: the unexpected sources of tissue regeneration" JOURNAL OF CLINICAL INVESTIGATION (2001), 107(11), 1355-1356 , 2001, XP002265781 *entire document* ----	1-28
A	TSAI, ROBERT Y. L. ET AL: "Plasticity, niches, and the use of stem cells" DEVELOPMENTAL CELL (2002), 2(6), 707-712 , 2002, XP009023173 *entire document* ----	1-28
	--- -/--	

INTERNATIONAL SEARCH REPORT

International Application No

PO 03/01098

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; BEILHACK, GEORG F. ET AL: "Purified allogeneic hematopoietic stem cell transplantation blocks diabetes pathogenesis in NOD mice" retrieved from STN Database accession no. 139:875 CA XP002265783 abstract & DIABETES (2003), 52(1), 59-68 , 2003,</p>	1-28
X	<p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 2002 ENDE NORMAN ET AL: "NOD/LtJ type I diabetes in mice and the effect of stem cells (Berashis) derived from human umbilical cord blood." Database accession no. PREV200300399271 XP002265784 abstract & JOURNAL OF MEDICINE (WESTBURY), vol. 33, no. 1-4, 2002, pages 181-187, ISSN: 0025-7850</p>	1-28

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

The present claims relate to further medical uses of a "regeneration initiating cell". This term is however not a well recognized term in the art and it is therefore impossible to establish the meaning and scope of the term. It is not clear in the sense of Article 6 PCT which cells are meant besides the ones described in the examples; i.e. bone-marrow, peripheral blood and human cord blood derived stem cells having certain surface markers. The application as a whole does not appear to support the use of any other cells than such cells, and the general term "regeneration initiating cell" is therefore not considered sufficiently disclosed in the sense of Article 5 PCT and clear in the sense of Article 6 PCT for any other cell.

A lack of clarity within the meaning of Article 6 PCT and a lack of sufficiency of disclosure within the meaning of Article 5 PCT therefore arise to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear, supported and sufficiently disclosed, namely medical uses of bone-marrow, peripheral blood and human cord blood derived stem cells possessing the markers according to claims 6 and 7 for treating pancreatic disorders.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 03/01098

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT 03/01098

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0111011	A	15-02-2001	AU 6621800 A CA 2381292 A1 EP 1226233 A2 JP 2003506075 T WO 0111011 A2	05-03-2001 15-02-2001 31-07-2002 18-02-2003 15-02-2001
WO 02064748	A	22-08-2002	EP 1367899 A2 WO 02064748 A2	10-12-2003 22-08-2002
EP 1254952	A	06-11-2002	AU 2228101 A CA 2395950 A1 EP 1254952 A1 AU 1055201 A AU 2695000 A WO 0148149 A1 WO 0148150 A1 WO 0148151 A1 US 2002142457 A1	09-07-2001 05-07-2001 06-11-2002 09-07-2001 09-07-2001 05-07-2001 05-07-2001 05-07-2001 03-10-2002
US 5780299	A	14-07-1998	AU 687386 B2 AU 6413994 A CA 2159804 A1 JP 2813467 B2 JP 8506735 T US 6008047 A WO 9423572 A1 US 5888816 A US 5646035 A US 5849584 A	26-02-1998 08-11-1994 27-10-1994 22-10-1998 23-07-1996 28-12-1999 27-10-1994 30-03-1999 08-07-1997 15-12-1998
WO 02083187	A	24-10-2002	US 2003031652 A1 WO 02083187 A1 US 2003099622 A1	13-02-2003 24-10-2002 29-05-2003